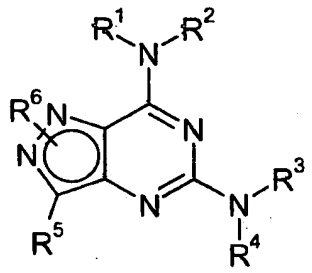
Claims

1. A compound of formula (I)



(I)

wherein

$R^1$ is a cyclic group selected from $R^A$, $R^B$, $R^C$ and $R^D$, each of which is optionally substituted with one or more $R^7$ groups;

$R^2$ is hydrogen or $C_1$-$C_2$ alkyl;

$R^3$ and $R^4$ are each independently $C_1$-$C_8$ alkyl, $C_2$-$C_6$ alkenyl, $C_2$-$C_8$ alkynyl or $C_3$-$C_{10}$ cycloalkyl, each of which is optionally substituted with one or more $R^8$ groups, or $R^E$, which is optionally substituted with one or more $R^9$ groups, or hydrogen;

or $-NR^3R^4$ forms $R^F$, which is optionally substituted with one or more $R^{10}$ groups;

$R^5$ is -Y-$CONR^{15}R^{16}$;

$R^6$, which may be attached at $N^1$ or $N^2$, is $C_1$-$C_6$ alkyl, $C_1$-$C_6$ haloalkyl, $C_2$-$C_6$ alkenyl or $C_2$-$C_6$ alkynyl, each of which is optionally substituted by $C_1$-$C_6$ alkoxy, $C_1$-$C_6$ haloalkoxy or a cyclic group selected from $R^J$, $R^K$, $R^L$ and $R^M$, or $R^6$ is $R^N$, $C_3$-$C_7$ cycloalkyl or $C_3$-$C_7$ halocycloalkyl, each of which is optionally substituted by $C_1$-$C_6$ alkoxy or $C_1$-$C_6$ haloalkoxy, or $R^6$ is hydrogen;

$R^7$ is halo, $C_1$-$C_6$ alkyl, $C_1$-$C_6$ haloalkyl, $C_2$-$C_6$ alkenyl, $C_2$-$C_6$ alkynyl, $C_3$-$C_{10}$ cycloalkyl, $C_3$-$C_{10}$ halocycloalkyl, phenyl, $OR^{12}$, $OC(O)R^{12}$, $NO_2$, $NR^{12}R^{13}$, $NR^{12}C(O)R^{13}$, $NR^{12}CO_2R^{14}$, $C(O)R^{12}$, $CO_2R^{12}$, $CONR^{12}R^{13}$ or CN;

$R^8$ is halo, phenyl, $C_1$-$C_6$ alkoxyphenyl, $OR^{12}$, $OC(O)R^{12}$, $NO_2$, $NR^{12}R^{13}$, $NR^{12}C(O)R^{13}$, $NR^{12}CO_2R^{14}$, $C(O)R^{12}$, $CO_2R^{12}$, $CONR^{12}R^{13}$, CN, $R^G$ or $R^H$, the last two of which are optionally substituted with one or more $R^9$ groups;

$R^9$ is $C_1$-$C_6$ alkyl, $C_1$-$C_6$ haloalkyl or $CO_2R^{12}$;

$R^{10}$ is halo, $C_3$-$C_{10}$ cycloalkyl, $C_3$-$C_{10}$ halocycloalkyl, phenyl, $OR^{12}$, $OC(O)R^{12}$, $NO_2$, $NR^{12}R^{13}$, $NR^{12}C(O)R^{13}$, $NR^{12}CO_2R^{14}$, $C(O)R^{12}$, $CO_2R^{13}$, $CONR^{12}R^{13}$, CN, oxo, $C_1$-$C_6$ alkyl or $C_1$-$C_6$ haloalkyl, the last two of which are optionally substituted by $R^{11}$;

$R^{11}$ is phenyl, $NR^{12}R^{13}$ or $NR^{12}CO_2R^{14}$;

$R^{12}$ and $R^{13}$ are each independently hydrogen, $C_1$-$C_6$ alkyl or $C_1$-$C_6$ haloalkyl;

$R^{14}$ is $C_1$-$C_6$ alkyl or $C_1$-$C_6$ haloalkyl;

$R^{15}$ and $R^{16}$ are each independently selected from
- hydrogen,
- $C_1$-$C_6$ haloalkyl,
- $C_1$-$C_6$ alkyl optionally substituted with
  - $R^{17}$,
  - $-NR^{18}R^{19}$,
  - $-CO_2R^{20}$,
  - $-CONR^{21}R^{22}$,
  - $R^{23}$ or
  - phenyl optionally substituted by
    - halo,
    - $C_1$-$C_6$ alkyl or
    - $R^{17}$,
- $C_3$-$C_7$ cycloalkyl optionally substituted with
  - $C_1$-$C_6$ alkyl,

$R^{17}$ or

$-NR^{18}R^{19}$, and

$R^{23}$;

or $NR^{15}R^{16}$ constitutes a 3- to 8-membered ring which may optionally include one or more further heteroatoms selected from nitrogen, oxygen and sulphur, and which may optionally be further substituted with $R^{17}$, $C_1$-$C_6$ haloalkyl, $-CO_2R^{20}$, $-CONR^{21}R^{22}$, oxo or $C_1$-$C_6$ alkyl optionally substituted by $R^{17}$;

$R^{17}$ is hydroxy, $C_1$-$C_6$ alkoxy, $C_1$-$C_6$ (haloalkyl)oxy or $C_3$-$C_7$ cycloalkyloxy;

$R^{18}$ and $R^{19}$ are each independently selected from hydrogen and $C_1$-$C_6$ alkyl;

or $-NR^{18}R^{19}$ constitutes an azetidine, pyrrolidine, piperidine or morpholine ring;

$R^{20}$ is hydrogen or $C_1$-$C_6$ alkyl;

$R^{21}$ and $R^{22}$ are each independently selected from hydrogen, $C_1$-$C_6$ alkyl, $C_1$-$C_6$ haloalkyl and $C_3$-$C_7$ cycloalkyl;

or $-NR^{21}R^{22}$ constitutes a 3- to 8-membered ring which may optionally include one or more further heteroatoms selected from nitrogen, oxygen and sulphur;

$R^{23}$ is a saturated 3- to 8-membered ring which includes at least one heteroatom selected from nitrogen, oxygen and sulphur, which ring may optionally be substituted by one or more $C_1$-$C_6$ alkyl groups, provided that the group $R^{23}$ is joined to the parent molecule by a covalent bond to a carbon atom of said ring;

$R^A$ and $R^J$ are each independently a $C_3$-$C_{10}$ cycloalkyl or $C_3$-$C_{10}$ cycloalkenyl group, each of which may be either monocyclic or, when there are an appropriate number of ring atoms, polycyclic and which may be fused to either

(a) a monocyclic aromatic ring selected from a benzene ring and a 5- or 6-membered heteroaromatic ring containing up to three heteroatoms selected from nitrogen, oxygen and sulphur, or

(b) a 5-, 6- or 7-membered heteroalicyclic ring containing up to three heteroatoms selected from nitrogen, oxygen and sulphur;

$R^B$ and $R^K$ are each independently a phenyl or naphthyl group, each of which may be fused to

(a) a $C_5$-$C_7$ cycloalkyl or $C_5$-$C_7$ cycloalkenyl ring,

(b) a 5-, 6- or 7-membered heteroalicyclic ring containing up to three heteroatoms selected from nitrogen, oxygen and sulphur, or

(c) a 5- or 6-membered heteroaromatic ring containing up to three heteroatoms selected from nitrogen, oxygen and sulphur;

$R^C$, $R^L$ and $R^N$ are each independently a monocyclic or, when there are an appropriate number of ring atoms, polycyclic saturated or partly unsaturated ring system containing between 3 and 10 ring atoms, of which at least one is a heteroatom selected from nitrogen, oxygen and sulphur, which ring may be fused to a $C_5$-$C_7$ cycloalkyl or $C_5$-$C_7$ cycloalkenyl group or a monocyclic aromatic ring selected from a benzene ring and a 5- or 6-membered heteroaromatic ring containing up to three heteroatoms selected from nitrogen, oxygen and sulphur;

$R^D$ and $R^M$ are each independently a 5- or 6-membered heteroaromatic ring containing up to three heteroatoms independently selected from nitrogen, oxygen and sulphur, which ring may further be fused to

(a) a second 5- or 6-membered heteroaromatic ring containing up to three heteroatoms selected from nitrogen, oxygen and sulphur;

(b) $C_5$-$C_7$ cycloalkyl or $C_5$-$C_7$ cycloalkenyl ring;

(c) a 5-, 6- or 7-membered heteroalicyclic ring containing up to three heteroatoms selected from nitrogen, oxygen and sulphur; or

(d) a benzene ring;

$R^E$, $R^F$ and $R^G$ are each independently a monocyclic or, when there are an appropriate number of ring atoms, polycyclic saturated ring system containing between 3 and 10 ring atoms, of which at least one is a heteroatom selected from nitrogen, oxygen and sulphur;

$R^H$ is a 5- or 6-membered heteroaromatic ring containing up to three heteroatoms independently selected from nitrogen, oxygen and sulphur; and

Y is a covalent bond, $C_1$-$C_6$ alkylenyl or $C_3$-$C_7$ cycloalkylenyl;

a tautomer thereof or a pharmaceutically acceptable salt, solvate or polymorph of said compound or tautomer.

2. A compound according to claim 1 wherein $R^1$ is $R^A$, which is optionally substituted with one or more $R^7$ groups; and
$R^A$ is a $C_3$-$C_{10}$ cycloalkyl group, which may be either monocyclic or, when there are an appropriate number of ring atoms, polycyclic, which may be fused to either

(a) a monocyclic aromatic ring selected from a benzene ring and a 5- or 6-membered heteroaromatic ring containing up to three heteroatoms selected from nitrogen, oxygen and sulphur, or

(b) a 5-, 6- or 7-membered heteroalicyclic ring containing up to three heteroatoms selected from nitrogen, oxygen and sulphur.

3. A compound according to claim 1 wherein $R^1$ is $R^B$, $R^C$, or $R^D$ each optionally substituted with one or more $R^7$ groups, wherein

$R^B$ is phenyl,

$R^C$ is a monocyclic saturated or partly unsaturated ring system containing between 5 and 7 ring atoms, of which at least one is a heteroatom selected from nitrogen, oxygen and sulphur,

$R^D$ is furanyl, thienyl, pyrrolyl, pyrazolyl, imidazolyl, isoxazolyl, oxazolyl, isothiazolyl, thiazolyl, oxadiazolyl, pyridyl, pyridazinyl, pyrimidyl or pyrazinyl, and

$R^7$ is fluoro, methyl, ethyl, hydroxy, methoxy, propoxy or CONHMe.

4. A compound according to any one of claims 1 to 3 wherein $R^2$ is hydrogen or methyl.

5. A compound according to any one of claims 1 to 4 wherein $R^3$ is hydrogen or $C_1$-$C_4$ alkyl, which is optionally substituted with one or more $R^8$ groups, or $R^3$ is azetidinyl, pyrrolidinyl or piperidinyl, each of which is optionally substituted with one or more $R^9$ groups, wherein

$R^8$ is hydroxy, methoxy, methoxyphenyl, $NH_2$, NHMe, $NMe_2$, $NHCO_2{}^tBu$, $NMeCO_2{}^tBu$, $CO_2H$, CONHMe, pyrrolidinyl, piperidinyl, morpholinyl or pyrazolyl, the last four of which are optionally substituted with one or more $R^9$ groups, and

$R^9$ is methyl or $CO_2{}^tBu$.

6. A compound according to any one of claims 1 to 5 wherein $R^4$ is hydrogen, methyl or ethyl.

7. A compound according to any one of claims 1 to 6 wherein $-NR^3R^4$ forms $R^F$, which is optionally substituted with one or more $R^{10}$ groups, wherein

$R^F$ is selected from azetidinyl, pyrrolidinyl, piperidinyl, piperazinyl, morpholinyl, 3-azabicyclo[3.1.0]hex-3-yl, homopiperazinyl, 2,5-diazabicyclo[4.3.0]non-2-yl, 3,8-diazabicyclo[3.2.1]oct-3-yl, 3,8-diazabicyclo[3.2.1]oct-8-yl, 1,4-diazabicyclo[4.3.0]non-4-yl and 1,4-diazabicyclo[3.2.2]non-4-yl, and

$R^{10}$ is halo, methyl, ethyl, isopropyl, hydroxy, methoxy, $NH_2$, NHMe, $NMe_2$, $NHCO_2{}^tBu$, $CO_2H$, $CO_2{}^tBu$, oxo, benzyl, $-CH_2NH_2$, $-CH_2NHMe$, $CH_2NMe_2$ or $-CH_2NMeCO_2{}^tBu$.

8. A compound according to any one of claims 1 to 7 wherein

$R^{15}$ and $R^{16}$ are each independently selected from hydrogen, $C_1$-$C_6$ alkyl optionally substituted with $R^{17}$, $-NR^{18}R^{19}$, $-CO_2R^{20}$, $-CONR^{21}R^{22}$, $R^{23}$ or phenyl optionally substituted by halo, $C_1$-$C_6$ alkyl or $R^{17}$, $C_3$-$C_7$ cycloalkyl and $R^{23}$, or $NR^{15}R^{16}$ constitutes a 5- to 7-membered ring which may optionally include one or more further heteroatoms selected from nitrogen and oxygen, and which may optionally be further substituted with $R^{17}$, $-CO_2R^{20}$, $-CONR^{21}R^{22}$ or $C_1$-$C_6$ alkyl optionally substituted by $R^{17}$;

$R^{17}$ is hydroxy, $C_1$-$C_6$ alkoxy or $C_3$-$C_7$ cycloalkyloxy;

$R^{21}$ and $R^{22}$ are each independently selected from hydrogen, $C_1$-$C_6$ alkyl, and $C_3$-$C_7$ cycloalkyl, or $-NR^{21}R^{22}$ constitutes a 5- to 8-membered ring which may optionally include one or more further heteroatoms selected from nitrogen and oxygen; and

$R^{23}$ is a saturated 5- to 7-membered ring which includes at least one heteroatom selected from nitrogen and oxygen, which ring may optionally be substituted by one or more $C_1$-$C_6$ alkyl groups.

9. A compound according to any one of claims 1 to 8 wherein $R^6$ is positioned on $N^1$.

10. A compound according to claim 9 wherein $R^6$ is hydrogen, methyl, ethyl, isopropyl, isobutyl, methoxyethyl, methoxypropyl, ethoxyethyl, ethoxypropyl, propoxyethyl, 2,2,2-trifluoroethyl, tetrahydrofuranylmethyl, tetrahydropyranylmethyl, tetrahydropyranyl or pyridinylmethyl.

11. A compound according to claim 1 wherein

$R^1$ is a cyclic group selected from $R^A$, $R^B$, $R^C$ and $R^D$, each of which is optionally substituted with one or more $R^7$ groups;

$R^7$ is halo, $C_1$-$C_6$ alkyl, $C_1$-$C_6$ haloalkyl, $OR^{12}$ or $CONR^{12}R^{13}$;

$R^8$ is halo, phenyl, $C_1$-$C_6$ alkoxyphenyl, $OR^{12}$, $NR^{12}R^{13}$, $NR^{12}CO_2R^{14}$, $CO_2R^{12}$, $CONR^{12}R^{13}$, $R^G$ or $R^H$, the last two of which are optionally substituted with one or more $R^9$ groups;

$R^A$ is a monocyclic $C_5$-$C_7$ cycloalkyl group;

$R^B$ is phenyl;

$R^C$ is a monocyclic saturated ring system containing between 5 and 7 ring atoms, of which at least one is a heteroatom selected from nitrogen, oxygen and sulphur;

$R^D$ is a 5-membered heteroaromatic ring containing a heteroatom selected from nitrogen, oxygen and sulphur and optionally up to two further nitrogen atoms in the ring, or a 6-membered heteroaromatic ring including 1, 2 or 3 nitrogen atoms;

$R^E$ is a monocyclic saturated ring system containing between 3 and 7 ring atoms containing one nitrogen atom;

$R^F$ is a monocyclic or, when there are an appropriate number of ring atoms, polycyclic saturated ring system containing between 3 and 10 ring atoms containing at least one nitrogen atom and optionally one other atom selected from oxygen and sulphur;

$R^G$ is a monocyclic saturated ring system containing between 3 and 7 ring atoms, of which at least one is a heteroatom selected from nitrogen, oxygen and sulphur; and

$R^H$ is a 5- or 6-membered heteroaromatic ring containing up to two nitrogen atoms.

$R^3$ is hydrogen, $C_1$-$C_4$ alkyl, which is optionally substituted with one or more $R^8$ groups, or $R^E$, which is optionally substituted with one or more $R^9$ groups;

$R^4$ is hydrogen, $C_1$-$C_6$ alkyl or $C_1$-$C_6$ haloalkyl;

or $-NR^3R^4$ forms $R^F$, which is optionally substituted with one or more $R^{10}$ groups;

$R^6$ is $C_1$-$C_4$ alkyl or $C_1$-$C_4$ haloalkyl, each of which is optionally substituted by $C_1$-$C_4$ alkoxy, $C_1$-$C_4$ haloalkoxy or a cyclic group selected from $R^J$, $R^L$ and $R^M$, or $R^6$ is $R^N$ or hydrogen;

$R^J$ is cyclopropyl or cyclobutyl;

$R^L$ and $R^N$ are each independently a monocyclic saturated ring system containing either 5 or 6 ring atoms, of which at least one is a heteroatom selected from nitrogen, oxygen and sulphur;

$R^M$ is a 5- or 6-membered heteroaromatic ring containing a heteroatom selected from nitrogen, oxygen and sulphur; and

Y is a covalent bond.

12. A compound according to claim 1 selected from:

1-(2-ethoxyethyl)-*N*-ethyl-5-(ethylamino)-7-(4-methylpyridin-2-ylamino)-1*H*-pyrazolo[4,3-*d*]pyrimidine-3-carboxamide,

5-(dimethylamino)-1-(2-ethoxyethyl)-*N*-methyl-7-(4-methylpyridin-2-ylamino)-1*H*-pyrazolo[4,3-*d*]pyrimidine-3-carboxamide,

5-(dimethylamino)-1-(2-ethoxyethyl)-*N*-(2-(methylamino)ethyl)-7-(4-methylpyridin-2-ylamino)-1*H*-pyrazolo[4,3-*d*]pyrimidine-3-carboxamide,

5-(dimethylamino)-*N*-(2-(dimethylamino)ethyl)-1-(2-ethoxyethyl)-7-(4-methylpyridin-2-ylamino)-1*H*-pyrazolo[4,3-*d*]pyrimidine-3-carboxamide,

5-(dimethylamino)-1-(2-ethoxyethyl)-7-(4-methylpyridin-2-ylamino)-*N*-(piperidin-4-yl)-1*H*-pyrazolo[4,3-*d*]pyrimidine-3-carboxamide,

5-(dimethylamino)-1-(2-ethoxyethyl)-*N*-(2-methoxyethyl)-7-(4-methylpyridin-2-ylamino)-1*H*-pyrazolo[4,3-*d*]pyrimidine-3-carboxamide,

(2*R*)-2-{[5-(dimethylamino)-1-(2-ethoxyethyl)-7-(4-methylpyridin-2-ylamino)-1*H*-pyrazolo[4,3-*d*]pyrimidine-3-carbonyl]amino}propionic acid,

3-{[5-(dimethylamino)-1-(2-ethoxyethyl)-7-(4-methylpyridin-2-ylamino)-1*H*-pyrazolo[4,3-*d*]pyrimidine-3-carbonyl]amino}propionic acid,

1-(2-ethoxyethyl)-*N*-methyl-7-(4-methylpyridin-2-ylamino)-5-(piperazin-1-yl)-1*H*-pyrazolo[4,3-*d*]pyrimidine-3-carboxamide,

1-(2-ethoxyethyl)-*N*-methyl-5-((3*R*)-3-methylpiperazin-1-yl)-7-(4-methylpyridin-2-ylamino)-1*H*-pyrazolo[4,3-*d*]pyrimidine-3-carboxamide,

1-(2-ethoxyethyl)-*N*-ethyl-5-((3*R*)-3-methylpiperazin-1-yl)-7-(4-methylpyridin-2-ylamino)-1*H*-pyrazolo[4,3-*d*]pyrimidine-3-carboxamide,

1-(2-ethoxyethyl)-5-(ethylamino)-*N*-methyl-7-(4-methylpyridin-2-ylamino)-1*H*-pyrazolo[4,3-*d*]pyrimidine-3-carboxamide,

1-(2-ethoxyethyl)-*N*-(2-methoxyethyl)-5-(methylamino)-7-(4-methylpyridin-2-ylamino)-1*H*-pyrazolo[4,3-*d*]pyrimidine-3-carboxamide,

5-(dimethylamino)-1-(2-ethoxyethyl)-*N*-(2-hydroxyethyl)-7-(4-methylpyridin-2-ylamino)-1*H*-pyrazolo[4,3-*d*]pyrimidine-3-carboxamide,

1-(2-ethoxyethyl)-5-(ethylamino)-*N*-(2-methoxyethyl)-7-(4-methylpyridin-2-ylamino)-1*H*-pyrazolo[4,3-*d*]pyrimidine-3-carboxamide,

1-(2-ethoxyethyl)-5-(*N*-(2-hydroxyethyl)-*N*-methylamino)-*N*-methyl-7-(4-methylpyridin-2-ylamino)-1*H*-pyrazolo[4,3-*d*]pyrimidine-3-carboxamide,

1-(2-ethoxyethyl)-5-((2-methoxyethyl)amino)-*N*-methyl-7-(4-methylpyridin-2-ylamino)-1*H*-pyrazolo[4,3-*d*]pyrimidine-3-carboxamide,

7-(cyclohexylamino)-1-(2-ethoxyethyl)-*N*-methyl-5-((3*R*)-3-methylpiperazin-1-yl)-1*H*-pyrazolo[4,3-*d*]pyrimidine-3-carboxamide, and

1-(2-ethoxyethyl)-*N*-methyl-5-[*N*-methyl-*N*-((3*S*)-1-methylpyrrolidin-3-yl)amino]-7-(4-methylpyridin-2-ylamino)-1*H*-pyrazolo[4,3-*d*]pyrimidine-3-carboxamide

and tautomers thereof and pharmaceutically acceptable salts, solvates and polymorphs of said compound or tautomer.

13. A pharmaceutical composition comprising a compound of formula (I) as claimed in any one of claims 1 to 12, or pharmaceutically acceptable salts, solvates or polymorphs thereof, and a pharmaceutically acceptable diluent or carrier.

14. A compound of formula (I) as claimed in any one of claims 1 to 12, or a pharmaceutically acceptable salt, solvate or polymorph thereof, for use as a medicament for the treatment of a disease or condition selected from hypertension (including essential hypertension, pulmonary hypertension, secondary hypertension, isolated systolic hypertension, hypertension associated with diabetes, hypertension associated with atherosclerosis, and renovascular hypertension), congestive heart failure, angina (including stable, unstable and variant (Prinzmetal) angina), stroke, coronary artery disease, congestive heart failure, conditions of reduced blood vessel patency (such as post-percutaneous coronary angioplasty), peripheral vascular disease, atherosclerosis, nitrate-induced tolerance, nitrate tolerance, diabetes, impaired glucose tolerance, metabolic syndrome, obesity, sexual dysfunction (including male erectile disorder, impotence, female sexual arousal disorder, clitoral dysfunction, female hypoactive sexual desire disorder, female sexual pain disorder, female sexual orgasmic dysfunction and sexual dysfunction due to spinal cord injury), premature labour, pre-eclampsia, dysmenorrhea, polycystic ovary syndrome, benign prostatic hyperplasia, bladder outlet obstruction, incontinence, chronic obstructive pulmonary disease, acute respiratory failure, bronchitis, chronic asthma, allergic asthma, allergic rhinitis, gut motility disorders (including irritable bowel syndrome), Kawasaki's syndrome, multiple sclerosis, Alzheimer's disease, psoriasis, skin necrosis, scarring, fibrosis, pain (particularly neuropathic pain), cancer, metastasis, baldness, nutcracker oesophagus, anal fissure and haemorrhoids.

15. Use according to claim 14 wherein the disease or condition is selected from essential hypertension, pulmonary hypertension, secondary hypertension, isolated systolic hypertension, hypertension associated with diabetes, hypertension associated with atherosclerosis, and renovascular hypertension.